UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/290,029	04/09/99	BOTTOMLY	H

HM12/0621

BRENDA HERSCHBACH JARRELL
CHOATE HALL & STEWART
EXCHANGE PLACE
53 STATE
BOSTON MA 02109-2891

EXAMINER	
EWOLDT, G	
ART UNIT	**PAPER NUMBER**
1644	7

DATE MAILED: 06/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/290,029	Bottomly et al.
Examiner	**Group Art Unit**
Gerald Ewoldt	1644

☒ Responsive to communication(s) filed on *Apr 6, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-281* is/are pending in the application.

Of the above, claim(s) *1-49, 56-59, 61-62, 67-78, 82-83, 92-93,* is/are withdrawn from consideration.

☐ ~~Claim(s)~~ *98-101, 105-107, 110, 113-114, 117-121, 124, 127-128, 130-135, 140-141, 151-152, 157-159, 176-183, 186-187, 192-281* ~~is/are allowed.~~

☒ Claim(s) *50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-109,* is/are rejected.

☐ ~~Claim(s)~~ *111-112, 115-116, 122-123, 125-126, 129, 136-139, 142-150,* ~~is/are objected to~~.

☐ ~~Claims~~ *153-156, 160-175, 184-185, 188-191* ~~are subject to restriction or election requirement.~~

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-281 are pending.

2. Applicant's election of Group XIV (claims 50-55, 60-61, 63-69, 79-98, 102-112, 115-117, 122-123, 125-127, 129, 136-157, 160-176, and 184-193) and the species:
a) pAPC - dendritic cell,
b) factor - CpG,
c) antigen - crude antigen preparation,
d) targeting agent - Fc receptor ligand,
e) encapsulating device - liposome
in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 50-55, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-109, 111-112, 115-116, 122-123, 125-126, 129, 136-139, 142-150, 153-156, 160-175, 184-185, and 188-191 read on the elected species of the elected invention and are being acted upon, wherein the elected invention comprises a method of modulating an immune system response to an antigen away from a Th2 response comprising isolating one or more pAPC from an individual and exposing said pAPC to an inducing agent factor concurrently with exposure to a protein antigen then administering said pAPC to a subject, said elected species consisting of:
a) pAPC - dendritic cell,
b) factor - CpG (Th1 inducing agent),
c) antigen - crude antigen preparation,
d) targeting agent - Fc receptor ligand,
e) encapsulating device - liposome

4. Claims 61, 67-69, 82-83, 92-93, 98, 105-107, 110, 117, 127, 140-141, 151-152, 157, 176, 186-187, and 192-193 (non-elected species from Group XIV) and 1-49, 56-59, 62, 70-78, 99-101, 113-114, 118-121, 124, 128, 130-135, 158-159, 177-183, and 194-281 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 50, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 109, 111-112, 115-116, 122-126, 129, 136-139, 142-150, 153-156, 160-175, 184-185, and 188-191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically:

A) Claims 50, 60, 63-66, 79-81, 84-91, 94-97, 102-104, 108-109, 111-112, 115-116, 122-126, 129, 136-139, 142-150, 153-156, 160-175, 184-185, and 188-191 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: administering isolated and exposed pAPC to a subject so as to modulate an immune response.

B) In claim 89, the term "administering" has no antecedent basis in base claim 64.

C) In claim 161, the term "mature pAPC" has no antecedent basis in base claim 160.

D) In claim 116 it is redundant to recite the term "selected from the group consisting of" twice.

E) Claim 108 depends on non-elected claim 101 and is therefore improper.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 50-55, 60, 64-66, 97, 102-104 108-109, 111-112, 115-116, 122-126, 129, 147, 156, 160-167, 175, and 191 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,126 in view of WO98/37919 and Romagnani (1997, IDS).

The '126 patent teaches a method of modulating an immune system response to an antigen comprising isolating pAPC (dendritic cells) from an individual and exposing said pAPC to a crude antigen followed by administering said pAPC to a subject (see particularly column 5 last paragraph - column 6 first paragraph; column 6, paragraph 10; and Example 4).

The reference teaching differs from the claimed invention in that it does not teach the modulation of the immune response away from a Th2 response (towards a Th1 response) and the generation of a specific set of cytokines (Th1) nor does it use a "factor", such as a CpG motif, with the antigen when exposing the pAPC to said antigen.

WO98/37919 teaches that an immune response can be redirected away from a Th2 response by directing it towards a Th1 response with the concurrent generation of a specific set of Th1 type cytokines. The reference also teaches the use of a CpG motif for the specific directing of a Th2 type immune response towards a Th1 type immune response and that the Th1 subset promotes delayed type hypersensitivity and cell-mediated immunity. Further the reference teaches the use of said method for the treatment of a disease or condition that would benefit from the redirection of an immune response (see particularly page 4, paragraph 3 and page 19 paragraphs 1-2).

Romagnani teaches that certain diseases and conditions are mediated by a Th1 type immune response while other diseases and conditions are mediated by a Th2 type immune response. Further the reference teaches that many allergic type immune responses are Th2 mediated (see particularly page 263, column 1, paragraph 1 and page 265 column 1, paragraph 1 - page 266 column 1, paragraph 1).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of modulating an immune system response to an antigen comprising isolating pAPC, exposing said pAPC to an antigen and a CpG motif "factor" (Th1 inducing agent), as taught by WO98/37919, followed by administration of said pAPC to a subject, as taught by the '126 patent, and to specifically direct said immune response away from a Th2 response towards a Th1 response, as taught by WO98/37919. One of ordinary skill in the art at the time the invention was made would have been motivated to perform said method as treatment for a Th2 mediated pathogenic condition (such as allergy) because said conditions are known to be Th2 mediated, as taught by Romagnani, and such a condition would benefit from the redirection of the immune response away from a Th2 response, as taught by WO98/37919.

9. Claims 63, 79-81, 84-86, 136-139, 142-144, 168-169, 184-185, and 188-190 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,126 in view of WO98/37919 and Romagnani (1997), as applied to claims 50-55, 60, 64-66, 97, 102-104, 108-109, 111-112, 115-116, 122-126, 129, 147, 156, 160-167, 175, and 191 above, and further in view of Maurer et al. (1997, IDS).

The '126 patent, WO98/37919, and Romagnani have been discussed supra.

The combined reference teachings differ from the claimed invention in that they do not additionally use a "targeting agent", such as an Fc receptor ligand, with the antigen when exposing the pAPC to said antigen.

Maurer et al. teach that an Fc receptor ligand can facilitate the uptake of antigen by a dendritic cell (see particularly page 176, paragraph 4).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of modulating an immune system response to an antigen comprising isolating pAPC, exposing said pAPC to an antigen concurrently with: a)a CpG motif "factor", as taught by WO98/37919, and b) a "targeting agent", as taught by Maurer et al., followed by administration of said pAPC to a subject, as taught by the '126 patent, and to specifically direct said response away from a Th2 response towards a Th1 response, as taught by WO98/37919. One of ordinary skill in the art at the time the invention was made would have been motivated to perform said method as treatment for a Th2 mediated pathogenic condition (such as allergy) because said conditions are known to be Th2 mediated, as taught by Romagnani, and such a condition would

benefit from the redirection of the immune response away from a Th2 response, as taught by WO98/37919. Additionally, one of ordinary skill in the art at the time the invention was made would have been motivated to combine an Fc receptor ligand "targeting agent" with the antigen to facilitate the uptake of said antigen by the dendritic cell, as taught by Maurer et al.

10. Claims 87-89, 145-146, 148, and 170-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,126 in view of WO98/37919, Romagnani (1997), as applied to claims 50-55, 60, 64-66, 97, 102-104, 108-109, 111-112, 115-116, 122-126, 129, 147, 156, 160-167, 175 and 191 above, and further in view of WO98/33520 (IDS).

The '126 patent, WO98/37919, and Romagnani have been discussed supra.

The combined reference teachings differ from the claimed invention in that they do not additionally use and "encapsulating device", such as a liposome, with the antigen when exposing the pAPC to said antigen.

WO98/33520 teaches the use of liposomes as encapsulating devices for antigens to increase their potency and clinical effectiveness (see particularly page 6 paragraph 3)

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of modulating an immune system response to an antigen comprising isolating pAPC, exposing said pAPC to an antigen concurrently with: a) a CpG motif "factor", as taught by WO98/37919, and b) a liposome "encapsulating device", as taught by WO98/33520, followed by administration of said pAPC to a subject, as taught by the '126 patent, and to specifically direct said response away from a Th2 response towards a Th1 response, as taught by WO98/37919. One of ordinary skill in the art at the time the invention was made would have been motivated to perform said method as treatment for a Th2 mediated pathogenic condition (such as allergy) because said conditions are known to be Th2 mediated, as taught by Romagnani, and such a condition would benefit from the redirection of the immune response away from a Th2 response, as taught by WO98/37919. Additionally, one of ordinary skill in the art at the time the invention was made would have been motivated to "encapsulate" said antigen-factor-targeting agent composition in a liposome to increase potency and clinical effectiveness, as taught by WO98/33520.

11. Claims 90-91, 94-96, 149-150, 153-155, 174, 184-185, and 188-190 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,126 in view of WO98/37919, Romagnani (1997), and WO98/33520, as applied to claims 50-55, 60, 64-66, 87-89, 97, 102-104, 108-109, 111-112, 115-116, 122-126, 129, 145-148, 156, 160-167, 170-173, 175, and 191 above, and further in view of Maurer et al. (1997).

The '126 patent, WO98/37919, Romagnani, and WO98/33520 have been discussed supra.

The combined reference teachings differ from the claimed invention in that they do not additionally use a "targeting agent", such as an Fc receptor ligand, with the antigen, "factor", and "encapsulating device", when exposing the pAPC to said antigen.

Maurer et al. teach that an Fc receptor ligand can facilitate the uptake of antigen by a dendritic cell (see particularly page 176, paragraph 4).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of modulating an immune system response to an antigen comprising isolating pAPC, exposing said pAPC to an antigen concurrently with: a)an Fc receptor ligand "targeting agent", as taught by Maurer et al., b) a CpG motif "factor", as taught by WO98/37919, and c) a liposome "encapsulating device", as taught by WO98/33520, followed by administration of said pAPC to a subject, as taught by the '126 patent, and to specifically direct said response away from a Th2 response towards a Th1 response, as taught by WO98/37919. One of ordinary skill in the art at the time the invention was made would have been motivated to perform said method as treatment for a Th2 mediated pathogenic condition (such as allergy) because said conditions are known to be Th2 mediated, as taught by Romagnani, and such a condition would benefit from the redirection of the immune response away from a Th2 response, as taught by WO98/37919. Additionally, one of ordinary skill in the art at the time the invention was made would have been motivated to "encapsulate" said antigen-factor-targeting agent composition in a liposome to increase potency and clinical effectiveness, as taught by WO98/33520. Further, one of ordinary skill in the art at the time the invention was made would have been motivated to combine an Fc receptor ligand "targeting agent" with the antigen to facilitate the uptake of said antigen by the dendritic cell, as taught by Maurer et al.

12. No claim is allowed.

13. WO98/33523, and the Bieber, De Vries, Fernandez et al., Grohmann et al., Hajek et al., Lotz et al., Tiandrawan et al., Van Den et al., Van Tendeloo et al., Zhang et al., and Ziegler et al. references have been lined through and have not been considered because they have not been provided by the Applicant. Additionally, Applicant must provide the source and year for the Ulmer et al. reference.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
June 19, 2000

Christina Chan
CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640